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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WOITACH, JOSEPH T	

ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action Summary	Application No.	Applicant(s)	
	09/944,448	LIM ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14, 25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

This application filed August 30, 2001 claims benefit to foreign applications: 2000-50881, filed August 30, 2000; 2000-65629, filed November 6, 2000; and 2001-12485, filed March 10, 2001 each filed in Korea.

Applicants' amendment filed June 16, 2003, paper number 8, has been received and entered. Claims 15-24 and 26-31 have been canceled. Claim 25 has been amended. Claims 1-14 and 25 are pending

Election/Restriction

Applicant's election of group I, claims 1-14 and 25 in Paper No. 8 (and previously in paper number 6) is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 1-14 and 25 are currently under examination as they are drawn to a method of establishing undifferentiated human embryonic stem cells in culture and the isolated undifferentiated human embryonic stem cells.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any

amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file (paper number 2). Should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d), a translation of the foreign application should be submitted under 37 CFR 1.55.

Specification

The nucleotide sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825. Applicant's attention is directed to the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998). In the instant case the present specification contains polynucleotide sequences which are used for primers (see for example lines bridging pages 28-29).

Appropriate correction is required.

The absence of proper sequence listing did not preclude the examination on the merits however, **for a complete response to this office action, applicant must submit the required material for sequence compliance.**

Claim Objections

Claim 2 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. In the instant case, claim 2 simply describes a human blastocyst embryo and is the same definition set forth in the specification at page 11, line 20 and art accepted description for a human blastocyst embryo.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for culturing the inner mass cells of a blastocyst embryo to establish embryonic stem cells, does not reasonably provide enablement for culturing any part of the blastocyst embryo. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case, the present specification does not provide any new methods for culturing embryos for the establishment of embryonic stem cells. Importantly, the present disclosure relies on the prior art for the specific methods of establishing embryonic stem cells from an embryo. Since the present disclosure relies on the art to practice the claimed invention it would also be subject to the same limitation recognized in the art. In the instant case, the only cells capable of establishing embryonic stem cells known in the art are the cells located in the

inner cell mass of the embryo. It is noted that the specification must teach those of skill in the art how to make and how to use the invention as broadly claimed. *In re Goodman*, 29 USPQ2d at 2013 (Fed. Cir. 1994), citing *In re Vaeck*, 20 USPQ2d at 1445 (Fed. Cir. 1991). The present specification provides no specific guidance for the establishment of embryonic stem cells from any other portion of the embryo as taught in the prior art besides the inner cell mass cells, therefore the ability to practice the instantly claimed methods would be limited to this art recognized embodiment.

In view of the lack of guidance, working examples, breadth of the claims, the level of skill in the art and state of the art at the time of the claimed invention was made, it would have required undue experimentation to make and/or use the invention as claimed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, claim 2 recites that the "human blastocyst embryo comprises a sphere of cells with an outer cell layer, a fluid cavity, and the inner cell mass" which is specifically set forth in the specification defining a blastocyst embryo. Moreover, this would be considered an art accepted description of a blastocyst embryo. The claims are unclear because

what the term "blastocyst embryo" encompasses in claim 1 is not clearly set forth if claim 2 would be considered to be further limiting.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 25 is rejected under 35 U.S.C. 102(b) as being anticipated by Thomson (1998- IDS reference).

Claim 25 encompasses an undifferentiated human embryonic stem cell formed by the method of claim 25. it si noted that the courts have stated that "When the structure recited in the reference is substantially identical to that of the claims, claimed properties or functions are presumed to be inherent." See MPEP 2112.01 or *In re Best*, 195 USPQ 430, 433 (CCPA 1997). In this case, while the embryonic stem cells are obtained from the method of claim 24, they are not materially different from an embryonic stem cell obtained by any other means. Thomson teaches the isolation and characterization of human embryonic stem cells. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art

products do not necessarily or inherently possess the characteristics of his claimed product. See *In re Ludtke*. Whether the rejection is based on "inherency" under 35 USC 102,, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. *In re Best, Bolton, and Shaw*, 195 USPQ 430, 433 (CCPA 1977) citing *In re Brown*, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972)

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Thomson (1998- IDS reference) with Kaufmann *et al.* Fert. Steril ((1995) 64:1125-1129).

Claim 1 encompasses broadly a method of making human embryonic stem cells from a cryopreserved blastocyst embryo. Dependent claims set forth more specific steps of how long the embryo is cryopreserved and method steps for thawing the frozen embryo. Presently, the only way to establish embryonic stem cells is by isolating and culturing the cells from the inner cell mass of an embryo. By example, Thomson *et al.* teach that human embryonic stem cells can be established from the human embryos (page 1145, middle column). The human embryos used by Thomson *et al.* were generated by IVF and preserved as frozen embryos (page 1145, top of middle column). However, the embryos used by Thomson *et al.* are cleavage stage embryos not blastocyst embryos as required by the instant claims. As exemplified by the source of embryos in Thomson *et al.* at the time of filing methods of cryopreserving embryos for clinical purposes were well known and routinely used in the art. At the time of filing Kaufmann *et al.* teach methods of cryopreserving human blastocyst stage embryos. Kaufmann *et al.* teach methods of cryopreserving human embryos. More specifically, Kaufmann *et al.* teach that embryos frozen at later stages of development serve as a better source of viable embryo than embryos preserved at earlier stages of development. While the method in general results in fewer embryos because development of the percentages of IVF embryos developing to later stages is less than the number of embryos formed by IVF, Kaufmann *et al.* teach that the embryos that are generated are of much better quality for further development as exemplified by the increase in implantation rate of embryos cryopreserved at the blastocyst stage (conclusion section). Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was

made to practice the methods of cryopreserving blastocyst embryos as taught by Kaufmann *et al.* as a means of generating and storing more viable embryos for later uses such as the use of the blastocyst for the formation of embryonic stem cells as taught by Thomson *et al.* Further, given that conditions of culturing, freezing and thawing of the embryo affect the resulting embryo, it would have been obvious to optimize conditions for each of these steps further to obtain viable embryos most suitable for further use. One having ordinary skill in the art would have been motivated to combine the methods of Thomson *et al.* with the methods of Kaufmann *et al.* because the resulting blastocyst required by Thomson *et al.* is more viable with the methods of Kaufmann *et al.* The additional steps for storage times and thawing of the cryopreserved embryos would have been obvious optimization steps of methods of embryo manipulation generally known and used in the art at the time of filing. There would have been a reasonable expectation of success given the results of Thomson *et al.* and Kaufmann *et al.* demonstrating the success of both of the steps encompassed by the claims.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Menzo *et al.* Human Reproduction, (1992) 7:101-106 is cited by Kaufmann *et al.* and teaches that optimization of culturing conditions for embryos/embryonic cells is required to obtain a proliferating viable embryonic cells.

Rall *et al.* Nature (1985) 313:573-575 provides further evidence that at the time of filing various methods of cryopreserving embryos were known and practiced in the art.

Piedrahita *et al.* (US Patent 6,271,436) teach methods of developing embryonic stem cells in other mammals which are similar to those used for human embryos.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141.

Joseph T. Woitach

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